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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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09/500,700 02/09/00 BARBAS III

C SCRI1160-4

EXAMINER

HM12/0828

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ART UNIT

PAPER NUMBER

1636

DATE MAILED:

08/28/01

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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.

09/500,700

Applicant(s)

BARBAS III ET AL.

Examiner

Gerald Leffers

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 11 June 2001.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 2-5, 16-19, 40 and 42-50 is/are pending in the application.
- 4a) Of the above claim(s) 47-50 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 2-5, 16-19, 40 and 42-46 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

DETAILED ACTION

Receipt is acknowledged of applicants' amendment, filed 6/11/01 as Paper No. 9, in which claims were cancelled (claims 6-15, 20-39 and 41), claims were amended (claims 3 and 40) and new claims added (claims 42-50). Claims 2-5, 16-19, 40 and 42-50 are pending in this application.

Receipt is also acknowledged of a supplemental copy of the paper sequence listing, CRF and attorney's statement as part of Paper No. 9. Finally, receipt is acknowledged of a supplemental information disclosure statement filed 6/11/01 as Paper No. 7. The signed and initialed PTO Form 1449 has been mailed along with this action.

Any rejection made of record in Paper No. 6 and not addressed in this action has been withdrawn. This action is Final.

Election/Restrictions

Applicant's election of Group I in Paper No. 9 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Applicants' amendment of the claims in Paper No. 9 includes several new claims which do not properly fall into the elected group. Newly submitted claims 47-50 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: claims 47-50 are drawn towards methods for isolating a zinc finger protein that binds to a target nucleic acid and are more properly included in the non-elected Group IV. Group IV is likewise drawn towards methods of isolating a zinc finger-nucleotide binding polypeptide variant. These methods are distinct from the zinc-finger nucleotide binding

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polypeptides of Group I for reasons of record in Paper No. 6. That a burdensome search would be required to examine claims 47-50 along with the members of Group I is demonstrated by their different patent classification.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 47-50 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03. Thus, while claims 2-5, 16-19, 40 and 42-50 are pending in this application, only claims 2-5, 16-19, 40 and 42-45 are under consideration.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 2-5, 16-19 are rejected under 35 U.S.C. 102(b) as being anticipated by Hanas et al (U; see the entire document). **This rejection is maintained for reasons of record in Paper No. 6.**

Response to Arguments

Applicant's arguments filed 6/11/01 in Paper No. 9 have been fully considered but they are not persuasive. Applicants' response essentially argues that applicants' invention differs from that of Hanas et al in that the zinc-finger proteins of the instant invention bind to a cellular

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nucleotide sequence different from the cellular nucleotide sequence which is bound by the parental zinc-finger protein(s) from which they are derived. According to applicants' response, the Hanas et al reference does not teach that their mutated zinc-finger proteins serve an additional function in gene expression. This appears to be an argument directed towards a limitation which is not actually in the rejected claims. Namely, that the variant zinc-finger polypeptide binds a polynucleotide sequence different from the sequence bound by the "parental" protein. Because claim 40 does appear to have such a limitation, the rejection of claim 40 as being anticipated by Hanas et al has been obviated.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 2, 4 and 16-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Crozatier et al (V; see the entire document). **This rejection is maintained for reasons of record in Paper No. 6.**

Response to Arguments

Applicant's arguments filed in Paper No. 9 have been fully considered but they are not persuasive. Applicants' response essentially argues 1) that the reference does not teach or suggest that the various mutations might be useful for enhancing or repressing gene expression, 2) there would have been no expectation of success in obtaining a mutant useful for regulation of gene expression, and 3) there is no limitation in the claimed invention that the retain the original binding activity before and after modification. The response appears to be arguing a motivation which was not presented as part of the original rejection and also appears to be arguing a limitation that is not present in the rejected claims. The motivation for isolating the mutant described by Crozatier et al was to characterize in vitro binding of DNA for the mutant relative to the wildtype polypeptide. No mention was made of enhancing or repressing gene expression. Nor is there such a limitation in the rejected claims. No evidence has been presented to indicate that there would not have been a reasonable expectation of success in isolating the mutant zinc-finger proteins constructed by Crozatier et al for use in in vitro characterization of their DNA-binding characteristics, as suggested by Crozatier et al. Because amended claim 40 comprises the limitation of binding to a second nucleic acid sequence, rejection of the claim as being obvious over Crozatier et al has been withdrawn.

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Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 2-5, 16-19 and 40 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-7, 21-22 and 53 of U.S. Patent No. 6,140,466. Although the conflicting claims are not identical, they are not patentably distinct from each other. **This rejection is maintained for reasons of record in Paper No. 6.**

Response to Arguments

Applicant's arguments filed in Paper No. 9 have been fully considered but they are not persuasive. Applicants' have deferred their response to this rejection until the claims of the instant application are otherwise in condition for allowance. The rejection is maintained because the grounds for rejection remain.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 42-46 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **This is a new rejection necessitated by applicants' amendments to the claims made in Paper No. 9.**

Each of the rejected claims is directed towards a "hybrid" zinc finger protein that binds to a target nucleic acid, the hybrid zinc finger comprising zinc fingers from a first protein linked to zinc fingers from a second protein. A reasonable interpretation of the claim language includes embodiments wherein at least two zinc fingers from a zinc finger protein of one type (e.g. Zif268) and two zinc fingers from a protein of another type (e.g. TFIIIA). The fingers can be "variants" of the parental donor fingers. The "variants" can be mutagenized forms of the parental donor fingers. The hybrid zinc finger protein can modulate expression of the target nucleic acid. The amino acid sequence of each finger can comprise two cysteines and two histidines with both cysteines are amino proximal to both histidines. The rejected claims thus encompass an enormous genus of possible combinations of zinc finger modules obtained from literally any zinc finger protein.

The specification exemplifies the zinc finger variants of the invention in terms of two known zinc finger proteins, Zif268 and TFIIIA. No other zinc finger proteins are described in detail in the specification. No description or relevant working example is provided wherein the zinc finger protein variant is a "hybrid" comprising fingers obtained from different types of proteins. In other words, no single embodiment of the claimed invention has been described in the specification. No significant description is provided of what such hybrid proteins would look

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like except to specify that the proteins would have zinc fingers obtained from different sources. The specification merely asserts that such recombinant hybrid proteins are feasible. No description is provided of which zinc finger modules from which sources would be desirable for recombination to produce a "hybrid" zinc finger protein. A single preferred linking domain, the 5 amino acid sequence TGEKP, is suggested for linking zinc finger modules in construction of the variant proteins of the invention. No other potential linking domain is described. No description is provided of other domains from any other zinc finger protein which would be retained in such a hybrid protein. Therefore, there is no basis provided by the specification for one of skill in the art to envisage a representative number of embodiments of the claimed invention.

The prior art does not appear to rectify the deficiencies of the instant specification regarding the claimed invention. The claimed invention does not appear to have been described in the prior art. While zinc finger proteins are and were known in the art, the combination of zinc finger modules to construct recombinant proteins does not appear to have been routinely practiced at the time of applicants invention.

Given the enormous number of potential hybrid zinc finger proteins encompassed by the rejected claims, derived from literally any zinc finger protein and recombined in any combination of fingers, and given the extremely limited description of such recombinant "hybrid" zinc finger proteins provided by the specification and prior art, one of skill in the art would not have been able to envisage a representative number of embodiments of such hybrid proteins to describe the claimed genus. Therefore, one of skill in the art would reasonably have concluded that applicants were not in possession of the claimed invention.

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The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 3 and 42-46 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. **These are new rejections necessitated by applicants' amendments to the claims in Paper No. 9.**

Claim 3 is vague and indefinite in that the preamble states that the claimed polypeptide is a "variant" of a zinc finger-nucleotide binding polypeptide, as claimed in claim 2, and is also selected from the group of Zif268 and TFIIIA. Zif268 and TFIIIA are known "wildtype" zinc finger proteins. It is not clear how the protein of claim 3 can be a "variant" zinc finger protein as described in claim 2 and also be one of the two known proteins recited in the Markush group of the claim. It would be remedial to amend the claim language to indicate that the claim protein is a variant of one of the two known proteins.

Claim 42 is vague and indefinite in that the metes and bounds of the phrase "...the hybrid zinc finger protein comprising zinc fingers from a first protein linked to zinc fingers from a second protein." are unclear. It is unclear whether the zinc fingers comprised within the hybrid protein must come from different types of zinc fingers (e.g. Zif268 and TFIIIA), or whether the hybrid can simply comprise multimers of zinc fingers from a single type of zinc finger protein (e.g. the multimers of Zif268 described in the specification). It would be remedial to amend the claim language to more clearly indicate whether the zinc fingers of the hybrid protein are necessarily obtained from proteins of different type.

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Conclusion

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Certain papers related to this application may be submitted to Art Unit 1636 by facsimile transmission. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. §1.6(d)). The official fax telephone numbers for the Group are (703) 308-4242 and (703) 305-3014. NOTE: If applicant does submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gerald Leffers, Jr. whose telephone number is (703) 308-6232. The examiner can normally be reached on Monday through Friday, from about 9:00 AM to about 5:30 PM. A phone message left at this number will be responded to as soon as possible (usually no later than 24 hours after receipt by the examiner).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's acting supervisor, Rob Schwartzman, Ph.D., can be reached at (703) 308-7307.

Any inquiry of a general nature or relating to the status of this application, or relating to attachments to this office action, should be directed to the Patent Analyst Zeta Adams, whose telephone number is (703) 305-3291.

AAZ
G. Leffers Jr., Ph.D.
Patent Examiner
Art Unit 1636
27 August 2001

David Guzo
DAVID GUZO
PRIMARY EXAMINER